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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/454,481	12/03/1999	JAMES P ALLISON	A-68668/RFT	3796

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EXAMINER	
RAWLINGS, STEPHEN L	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 12/05/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/454,481	ALLISON ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 November 2001 and 28 May 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-21,23-25,27,28 and 31* is/are pending in the application.

4a) Of the above claim(s) *13-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21,23-25,27,28 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *13-21,23-25,27,28 and 31* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The amendment filed May 28, 2002 in Paper No. 15 is acknowledged and has been entered. Claims 22, 26, 29, 30, and 32 have been canceled. Claims 21, 23-25, 27, and 31 have been amended.

2. The amendment filed November 23, 2001 in Paper No. 12 is acknowledged and has been entered.

3. Claims 13-21, 23-25, 27, 28, and 31 are pending in the application. Claims 13-20 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention.

4. Claims 21, 23-25, 27, 28, and 31 are currently under prosecution.

Grounds of Claim Rejections Withdrawn

5. Unless specifically reiterated below, the grounds of claim rejections set forth in the previous Office action mailed May 22, 2001 (Paper No. 10) have been withdrawn.

Grounds of Claim Rejections Maintained and Reply to Applicants' Remarks

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 21, 23-25, 27, 28, and 31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for inhibiting the growth of non-T cell tumor cells in a mouse, wherein said method comprises a step of administering a self antigen preparation to the mouse and the hamster anti-mouse

CTLA-4 monoclonal antibody 9H10, does not reasonably provide enablement for a method for inhibiting the growth of a non-T cell tumor cells in any mammal, wherein said method comprises contacting at least one of the mammal's T cells with a self antigen preparation and a CTLA-4 blocking agent that specifically binds the extracellular domain of CTLA-4 and inhibits CTLA-4 signaling. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims for the reasons set forth in the previous Office action mailed May 22, 2001 (Paper No. 10).

Applicants have traversed these grounds of rejection in Paper No. 12. Applicants' arguments have been carefully considered but have not been found persuasive.

In reply to Applicants' argument that the references cited as a basis of rejection do not address the use of a CTLA-4 blocking agent, Applicants are directed to Sotomayer, et al, Christadoss, et al, Sullivan, et al, Zhu, et al, Chambers, et al, Gribben, et al, Anderson, et al, and Yang, et al, which contrary to Applicants' remarks, were cited in the previous Office action and address the problems associated with the use of a CTLA-4 blocking agent. In reply to Applicants' argument that these particular references are improperly cited, the teachings of the references provide a reasonable and sound scientific basis for rejection of the claims under 35 USC § 112, first paragraph. In addition, contrary to Applicants' contentions, given only the benefit of the Applicants' instant disclosure, the skilled artisan would not have a reasonable expectation of successfully making and using the claimed invention without the need to perform additional, undue experimentation. Moreover, because one would reasonably imagine that the claims encompass many non-working embodiments, which could not be identified by any means other than producing a species of a putative CTLA-4 blocking agent, determining whether or not the species specifically binds CTLA-4, determining whether or not the species can inhibit CTLA-4 signaling and then determining whether or not the species can be used to effectively inhibit the growth of non-T cell tumors in a mammal, finding the working embodiments among the possibilities would require undue experimentation.

In further reply to Applicants' remarks, although Applicants are not required under the statutes, or by the Patent and Trademark Office to seek or secure approval by the Food and Drug Administration to use the claimed invention in order to attain patent rights for their invention, Applicants are required to meet the enablement requirements set forth under 35 USC § 112, first paragraph. In view of the preponderance of evidence, which has been made of record in established a case for the insufficiency of the specification to meet the requirements set forth under 35 USC § 112, first paragraph, it is not immediately apparent that these requirements have been met, and therefore Applicants have the burden of persuading the Office that given only the benefit of the instant disclosure the skilled artisan could have used the claimed invention with a reasonable expectation of success without the need to perform additional, undue experimentation at the time the application was filed.

The courts addressed the issue of the amount of experimentation that is or is not undue; see *In re Brana*, 34 USPQ2d 1436, CAFC 1995. The situation faced by Applicants in the course of the instant prosecution is not analogous to that faced by Brana, et al, since notably Applicants have not established the clinical utility of the claimed invention, nor have Applicants provided a reasonably correlative study suggesting the potential utility of the claimed invention. Accordingly, in the present regard, it is not merely a question of whether or not a favorable comparison of the claimed invention and proven effective antitumor therapeutic compounds implicitly asserts that the invention is also highly effective against cancer, or whether such a disclosure can be reasonably extrapolated to reliably predict the efficacy of the claimed invention encompassing clinical application. Furthermore, the factors, which have been considered in determining whether undue experimentation would be required, have been summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). Considering the nature of the invention, the state of the art at the time the application was filed, the level of skill in the art, the level of predictability in the art, the breadth of the claims and the amount of exemplification disclosed by Applicants, the quantity and type of experimentation that would be required before the claimed invention might be practiced with a reasonable expectation of success in view of such factors is considered undue.

In contrast to the situation faced by Brana, et al, in order to practice the claimed invention in this instance, the skilled artisan would not merely be required to perform routine experimentation using conventional methodology to determine optimally safe and effective dosages and schedules for administration. Contrary to the situation faced by Brana, et al, in this instance, there does not appear to be a reasonable presumption of the clinical utility of the claimed invention.

In conclusion, Applicants' arguments have been carefully considered but in view of the preponderance of evidence of record, the stated grounds of rejection under 35 USC § 112, first paragraph are maintained.

8. Claims 21, 23-25, 27, 28, and 31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons set forth in the previous Office action mailed May 22, 2001 (Paper No. 10).

To briefly reiterate the stated grounds of rejection, as broadly written, the claims encompass a method for treatment of mammals with an undisclosed agent, wherein said agent can be a peptide, a peptidomimetic, a small organic molecule, a soluble T cell receptor, a polyclonal antibody, a monoclonal antibody or antigen-binding fragment thereof, or any other agent that specifically binds the extracellular domain of CTLA-4 and is inhibitory of signaling activity associated with CTLA-4. However, a detailed description of at least substantial and representative number of members of the genus of CTLA-4 blocking agents to which the claims refer has not been included in the specification to reasonably convey to one skilled in the art that Applicants had possession of the invention at the time the application was filed.

Applicants have traversed these grounds of rejection in Paper No. 12. Applicants' arguments have been carefully considered but have not been found persuasive. According to MPEP § 2163.02, "[a]n objective standard for determining compliance with the written description requirement is, 'does the description clearly

allow persons of ordinary skill in the art to recognize that he or she invented what is claimed' ". Furthermore, the courts have decided:

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed*.

See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Accordingly, so that one of ordinary skill in the art given benefit of the disclosure, would recognize that Applicants invented that which is claimed in the application, the disclosure must describe the subject matter encompassed by the claims in sufficient detail to reasonably convey to the skilled artisan that the Applicants had possession of that subject matter at the time the application was filed. Therefore, contrary to Applicants' arguments, to meet the written description requirement, the disclosure must do more than merely describe a means for making and using the invention. To meet the written description requirement, the disclosure must include a description of at least a substantial, or at least a representative number of embodiments of the methods encompassed by the claims, and of sufficient detail to satisfy a factual inquiry to determine whether the skilled artisan would have reasonable cause given only benefit of Applicants original disclosure, to accept the assertion set forth in the claims that Applicants had possession of the claimed invention as of the filing date sought.

The present disclosure does not include a description of at least a substantial number of embodiments of the methods encompassed by the claims, and does not include a description of at least a representative number of embodiments of the methods encompassed by the claims, and the descriptions of the embodiments that are included are not of sufficient detail to satisfy the factual inquiry, as the skilled artisan given only the benefit of the disclosure, would not reasonably conclude that Applicants had possession of the claimed invention at the time the application was filed. Therefore, although Applicants' arguments have been carefully considered, the disclosure is considered insufficient to meet the written description requirement of 35 USC § 112, first paragraph.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 21, 23-25, 27, 28, and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 21, 23-25, 27, 28, and 31 are indefinite because claim 21 does not recite a positive process step. Accordingly, one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention. As previously noted, amending claim 21 to recite, for example, the phrase "whereby the growth of non-T cell tumor cells in the host is inhibited" can obviate this rejection.

In Paper No. 12, Applicants have requested withdrawal of this ground of rejection in view of the amendment filed therewith. However, presently claim 21 still does not recite a positive process step that clearly related back to the preamble of the claim and therefore the stated ground of rejection under 35 USC § 112, second paragraph is maintained.

(b) Claims 21, 23-25, 27, 28, and 31 are indefinite because claim 21 recites the phrase "characterized as specifically binding to the extracellular domain of CTLA-4 and inhibitory of CTLA-4 signaling". As noted in the previous Office action, the use of the phrase renders the claims indefinite because it is unclear whether the claim requires the CTLA-4 blocking agent to specifically bind the extracellular domain of CTLA-4 or to be merely characterized as having the potential of doing so. Furthermore, recitation of the phrase renders the claims indefinite because it is unclear whether the claim requires the CTLA-4 blocking agent to specifically inhibit CTLA-4 signaling or to merely be characterized as having the potential of doing so. Additionally, it is unclear whether the claim requires the CTLA-4 blocking agent to inhibit CTLA-4 signaling upon specifically binding the extracellular domain of CTLA-4, or if the CTLA-4 blocking agent merely has to be capable of both activities.

Applicants have traversed this ground of rejection in Paper No. 12 arguing that one of ordinary skill in the art would be reasonably apprised of the metes and bounds of the present claims. Applicants' arguments have been carefully considered but have not been found persuasive, as due to the ambiguity associated with the language of the present claims, the present claims fail to distinctly claim and particularly point out the subject matter that Applicants regard as the invention. Therefore the stated ground of rejection under 35 USC § 112, second paragraph is maintained.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

12. Claims 21, 23, and 27 are rejected under 35 U.S.C. § 102(a) as being anticipated by Leach, et al (*Science* **271**: 1734-1736, 1996) for the reasons set forth in the previous Office action mailed May 22, 2001 (Paper No. 10).

Applicants have traversed this ground of rejection under 35 USC § 102(a) arguing that Leach, et al does not anticipate the claimed invention. Applicants' argument has been considered but has not been found persuasive. The teachings of Leach, et al anticipate the claimed invention, as Leach, et al teach a method comprising contacting at least one T cell in a mammal with a self antigen preparation, namely a vaccine composed of tumor cells, and a CTLA-4 blocking agent. Thus the claimed method is anticipated because the method will inherently lead to breaking immune tolerance, stimulating an autoreactive T cell response against a self antigen expressed on non-T cell tumor cells, and inhibiting the growth of the non-T cell tumor cells. See *Ex parte Novitski*, 26 USPQ 1389 (BPAI 1993).

13. Claims 21, 23-25, 27, and 28 are rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 5,811,097 A for the reasons set forth in the previous Office action mailed May 22, 2001 (Paper No. 10).

Applicants have traversed the ground of this rejection arguing that the cited reference does not anticipate the claimed invention because it does not teach or suggest an autoreactive T cell response. As noted in the previous Office action, the method of U.S. Patent No. 5,811,097 A comprises the same method steps as claimed in the instant invention, that is, at least one of a mammal's T cells with a tumor vaccine and a CTLA-4 blocking agent. Thus the claimed method is anticipated because the method will inherently lead to conferring growth inhibition upon tumor cells. By the same token, in reply to Applicants' remarks, the claimed method is anticipated because the method will inherently lead to activation of autoreactive T cells against cells expressing the self-antigens, including the non-T cell tumor cells of which the tumor vaccine is composed.

14. Claims 21, 23-25, 27, and 28 are rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 5,855,887 A for the reasons set forth in the previous Office action mailed May 22, 2001 (Paper No. 10).

Applicants have traversed the ground of this rejection arguing that the cited reference does not anticipate the claimed invention because it does not teach or suggest an autoreactive T cell response. As noted in the previous Office action, the method of U.S. Patent No. 5,855,887 A comprises the same method steps as claimed in the instant invention, that is, at least one of a mammal's T cells with a tumor vaccine and a CTLA-4 blocking agent. Thus the claimed method is anticipated because the method will inherently lead to conferring growth inhibition upon tumor cells. By the same token, in reply to Applicants' remarks, the claimed method is anticipated because the method will inherently lead to activation of autoreactive T cells against cells expressing the self-antigens, including the non-T cell tumor cells of which the tumor vaccine is composed.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. Claims 21, 23-25, 27, 28, and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leach, et al (*Science* **271**: 1734-1736, 1996) in view of Heslop (*Baillieres Clinical Haematology* **7**: 135-151, 1994), Sussman, et al (*Annals of Surgical Oncology* **1**: 296-306, 1994), and Wallack, et al (*Mt. Sinai Journal of Medicine* **59**: 227-233, 1992) for the reasons set forth in the previous Office action mailed May 22, 2001 (Paper No. 10).

Applicants have traversed this ground of rejection in Paper No. 12. Applicants' arguments have been carefully considered but have not been found persuasive. Contrary to Applicants' assertions, given the teachings of the cited prior art, the invention would have been obvious to one of ordinary skill in the art at the time the invention was made. Moreover, the artisan would have been motivated at the time the invention was made to derive the invention given the teachings of the prior art.

17. Claims 21-25, 27-29, and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,811,097 A for the reasons set forth in the previous Office action mailed May 22, 2001 (Paper No. 10).

Applicants have traversed this ground of rejection in Paper No. 12. Applicants' arguments have been carefully considered but have not been found persuasive. Contrary to Applicants' assertions, given the teachings of the cited prior art, the invention would have been obvious to one of ordinary skill in the art at the time the invention was made. Moreover, the artisan would have been motivated at the time the invention was made to derive the invention given the teachings of the prior art.

18. Claims 21-25, 27-29, and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,855,887 A for the reasons set forth in the previous Office action mailed May 22, 2001 (Paper No. 10).

Applicants have traversed this ground of rejection in Paper No. 12. Applicants' arguments have been carefully considered but have not been found persuasive. Contrary to Applicants' assertions, given the teachings of the cited prior art, the invention would have been obvious to one of ordinary skill in the art at the time the invention was made. Moreover, the artisan would have been motivated at the time the invention was made to derive the invention given the teachings of the prior art.

Double Patenting

19. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

20. Claims 21, 22-25, 27, and 28 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3, 4, 6, 8, 18,

and 20 of U.S. Patent No. U.S. Patent No. 6,051,227 A. Although the conflicting claims are not identical, they are not patentably distinct from each other for the reasons set forth in the previous Office action mailed May 22, 2001 (Paper No. 10).

Applicants have traversed this ground of rejection in Paper No. 12. In reply to Applicants' argument, the subject matter of the claims of the patent is anticipatory of the subject matter claimed in this application. Therefore, although Applicants' arguments have been carefully considered, the rejection of claims 21, 22-25, 27, and 28 for the reasons set forth in the previous Office action is maintained.

21. Claims 21, 22-25, 27, 28, and 31 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3, 4, 6, 8, 18, and 20 of U.S. Patent No. 6,051,227 A in view of Heslop (*Baillieres Clinical Haematology* **7**: 135-151, 1994) for the reasons set forth in the previous Office action mailed May 22, 2001 (Paper No. 10).

Applicants have traversed this ground of rejection in Paper No. 12. In reply to Applicants' argument, the subject matter of the claims of the patent is anticipatory of the subject matter claimed in this application, or would have been obvious to one of ordinary skill in the art at the time the application was filed given benefit of the teachings of the prior art. Therefore, although Applicants' arguments have been carefully considered, the rejection of claims 21, 22-25, 27, 28, and 31 for the reasons set forth in the previous Office action is maintained.

22. Claims 21, 23, 25, 27, and 31 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 6-11 of U.S. Patent No. 5,811,097 A. Although the conflicting claims are not identical, they are not patentably distinct from each other for the reasons set forth in the previous Office action mailed May 22, 2001 (Paper No. 10).

Applicants have traversed this ground of rejection in Paper No. 12. In reply to Applicants' argument, the subject matter of the claims of the patent is anticipatory of the subject matter claimed in this application. Therefore, although Applicants' arguments

have been carefully considered, the rejection of claims 21, 23, 25, 27, and 31 for the reasons set forth in the previous Office action is maintained.

23. Claims 21, 23-25, 27, and 31 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 6-11 of U.S. Patent No. 5,811,097 A in view of Heslop (*Baillieres Clinical Haematology* **7**: 135-151, 1994) for the reasons set forth in the previous Office action mailed May 22, 2001 (Paper No. 10).

Applicants have traversed this ground of rejection in Paper No. 12. In reply to Applicants' argument, the subject matter of the claims of the patent is anticipatory of the subject matter claimed in this application, or would have been obvious to one of ordinary skill in the art at the time the application was filed given benefit of the teachings of the prior art. Therefore, although Applicants' arguments have been carefully considered, the rejection of claims 21, 23-25, 27, and 31 for the reasons set forth in the previous Office action is maintained.

New Grounds of Rejection

Claim Rejections – 35 USC § 112

24. Claims 24 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 24 is vague and indefinite because the claim recites the limitation "capable of expressing". Recitation of the limitation renders the claim vague and indefinite because it cannot be ascertained whether the claim requires the tumor cells to be transduced with a nucleic acid construct that expresses a cytokine, or merely transduced with a nucleic acid construct that could be used to express a cytokine and therefore is "capable of expressing" a cytokine. For example, it is unclear whether Applicants regard a method wherein said tumor cells are transduced with an "empty" expression vector, which is merely capable of expressing a polynucleotide sequence

encoding a cytokine, to be part of the invention. Accordingly, one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

Conclusion

25. No claims are allowed.

26. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

27. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (703) 305-3008. The examiner can normally be reached on Monday-Thursday, alternate Fridays, 8:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C. Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Stephen L. Rawlings, Ph.D.
Art Unit 1642

slr
December 3, 2002

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER